EUROPEAN UNION

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Second Medical Uses and Supplementary Protection Certificates. No means No.

Introduction

In the development of drugs, it is often found that the active ingredient being investigated has unexpected effects. Some effects are good (i.e. a new medical indication or a second medical use) and some bad (i.e. side effects). It has long been the case under the European Patent Convention that where a known active ingredient has been found to have a second medical use, then the ingredient can be patented for that use.[1] Whether it is a first or second medical use, the road to market is a long one because before any new medical product can be sold it needs a marketing authorisation ("MA") (usually) from the European Medicines Agency ("EMA"). And to get an authorisation it is necessary for the drug to be found to be safe and efficacious by way of clinical and other trials. Critically, it is necessary to obtain a new MA from the EMA for a product each time it is to be sold for a new use, in a new dose, or in a new method of administration.

However, the European Union[2] makes it possible to, in effect, extend the term of a patent to give back some of the period of exclusivity lost due to regulatory delays.[3] This is done by way of obtaining a supplementary protection certificate ("SPC").[4] A SPC gives patent-like protection for up to five and half years after the expiry of the patent.[5] The regime which is, in principle, quite straightforward has become convoluted and complex after 45 decisions of the Court of Justice of the European Union[6] and many more in respective national courts. But it remains easy to express the four requirements for obtaining a SPC:

> (a) the product is protected by a basic patent in force;
>
> (b) there is a valid authorisation to place the product as a medicinal product has been granted in accordance with the relevant approval regime;[7]
>
> (c) the product has not already been the subject of a SPC; and
>
> (d) the authorisation is the first authorisation to place the product on the market as a medicinal product.

Furthermore, the term of the SPC is calculated as the period equal to that which elapsed between the filing date of the patent and the date of the "first" authorisation to place the product on the market in the European Economic Area (minus five years).[8] Thus, identifying the "first" authorisation is determinative for both eligibility for a SPC and also its duration.

So how should the words "first authorisation" be interpreted? Put simply, is the "first" authorisation the first authorisation for the active ingredient with any indication or the first authorisation for a particular indication? The recent decision in C-181/24 *Genmab A/S* ("*Genmab*")[9] is the latest step in the saga in determining what counts as the "first" but let's begin with some background.

"First" authorisation

When the issue first came before the Court of Justice in C-31/03 *Pharmacia Italia* ("*Pharmacia*"),[10] the Court said that the intended use of the medical product was not the decisive factor in determining which authorisation was "first". A veterinary use is the "first" even where there is a subsequent human use. So only the first medical indication would obtain a certificate even where a subsequent indication is more useful and so more profitable.

This narrow view of what amounts to the "first" authorisation was explored again in C-130/11 *Neurim Pharmaceuticals (1991) Ltd v Comptroller-General of Patents* ("*Neurim*").[11] In this case, without referring back to *Pharmacia*, the Court of Justice held:

> *only the MA of the first medicinal product comprising the product and authorised for a therapeutic use corresponding to that protected by the patent relied upon for the purposes of the application for the SPC, may be considered to be the first MA of "that product".*[12]

Thus, for a while, the "first" authorisation was that for a particular indication and so certificates were potentially available for each medical indication covered by a patent (or patents). But this liberal approach presented challenges regarding how the SPC system could be reconciled with other decisions of the Court.[13]

The story continued with C-443/17 *Abraxis Bioscience*[14] where the Court held that the meaning of "first" authorisation should be narrowly interpreted.[15] Accordingly, an authorisation for a new formulation of an old authorised active ingredient cannot be regarded as being the "first" granted for that product as a medicinal product.[16] This was confirmed in C-673/18 *Santen SAS* ("*Santen*")[6] where it was said that the first authorisation is that which first includes the product incorporating the active ingredient irrespective of any therapeutic indication.[17] Thus, *Neurim* was overturned[18] and the approach in *Pharmacia* was restored. *Santen* was aiming for simplicity. And the approach the Court put forward meant there was no need to look beyond the listed active ingredient to decide whether a MA was the "first".

However, is there anything a drug developer can do where the second medical indication is discovered many years later, or even, where is has a wider application across the population? The Court of Justice had to consider one work-around when ofatumumab was approved for the second time and the patent proprietor, Genmab, applied for a SPC.

Ofatumumab

On 21 April 2010, Genmab[19] obtained a MA for its drug ofatumumab for use in a therapy for untreated chronic lymphocytic leukaemia.[20] This is a rare disease which was even given "orphan" designation. This designation gives certain advantages to the company marketing the drug, but it also means that it is less likely to be profitable. On 28 February 2019, this MAwas withdrawn for "commercial reasons",[21] namely the product was being withdrawn from the market. Subsequently, on 29 March 2021, Genmab obtained a MA for using ofatumumab for the treatment of relapsing-remitting multiple sclerosis.[22] Thereafter, Genmab applied for a SPC on 7 July 2021 based on this MA and its patent.[23] This application was refused on the basis the "first" MA was that granted in 2010.

Genmab argued that as the earlier authorisation had been withdrawn it was no longer the "first", rather, it said, the "first" authorisation is the earliest that which was still in force (valid) at the time of the application.[24] The Court of Justice took the view that a granted authorisation remains the "first" whether or not it is still in force. Its reasons were based on the normal reading of the relevant provision[25] and it took the view that taking into account only "in force"

or "valid" MAs would mix up other concepts.[26] It went on to reiterate that the regime was set up:

> *to protect not all pharmaceutical research giving rise to the grant of a patent and the marketing of a medicinal product, but to protect only research leading to the first MA of an active ingredient as a medicinal product* [27]

This outcome would be undermined if it were sufficient to withdraw a MA to make it the "first". Indeed, while not raised by the Court, it would be problematic if a less profitable (but useful) drug was withdrawn from the market (by withdrawing the authorisation) because a pharmaceutical company favours a more profitable product. Not to mention if this sort of strategy were permitted it might encourage anti-competitive behaviour.[28]

Conclusion

The *Genmab* decision, in itself, was unsurprising. The Court once more confirming its stance that the regime for obtaining SPCs should be simple. And that certificates are not available for second medical uses. The difficulty with this strict approach is that it means the SPC regime provides no incentive to develop further medical uses of known active ingredients.[29] But maybe the patent, and other mechanisms, such as data exclusivity, are sufficient. Time will tell.

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[1] European Patent Convention, art 54(4) (introduced in EPC 2000, but "Swiss form" claims were acceptable following G 5/83 *Second Medical Use/EISAI* [1985] OJ EPO 64).
[2] And the European Economic Area and, also, still in the United Kingdom.
[3] For a more detailed discussion of the regime see *Roughton, Johnson and Cook on Patents* (5th ed, Butterworths 2022), ch 22.
[4] Regulation (EC) No 469/20095 concerning supplementary protection certificates for medicinal products; a parallel regime exists for plant protection products: Regulation (EC) No 1610/96 concerning supplementary protection certificates for plant protection products.
[5] The extra six months beyond five years is only available where a paediatric investigation plan is lodged.
[6] This is based on the number of cases included in the category list on <www.ipcuria.eu>.
[7] Directive 2001/83/EC on the Community code relating to medicinal products for human use or Directive 2001/82/EC on the Community code relating to veterinary medicinal products.
[8] Regulation (EC) No 469/2009, art 13(1).
[9] EU:C:2024:627.
[10] [2004] ECR I-1001, [20].
[11] EU:C:2012:489.
[12] C-130/11 *Neurim Pharmaceuticals (1991) Ltd v Comptroller-General of Patents* EU:C:2012:489, [26].
[13] See comments of Arnold J in *Abraxis Bioscience Llc v The Comptroller-General of Patents* [2017] EWHC 14 (Pat), [37] and [38].
[14] EU:C:2019:238.
[15] C-443/17 *Abraxis Bioscience LLC* EU:C:2019:238, [34] and [37].
[16] C-443/17 *Abraxis Bioscience LLC* EU:C:2019:238, [40] and [44].
[17] C-673/18 *Santen SAS* EU:C:2020:531, [51].
[18] The English courts did not return to the approach in *Neurim* when it was presented with the opportunity to do so in *Newron Pharmaceuticals SPA v The Comptroller General of Patents* [2024] EWCA Civ 128.
[19] This was how it was put by the Court of Justice, but it was much more complicated due to changes of ownership and so forth: see C-181/24 *Genmab A/S*, EU:C:2024:627, [13].
[20] See 'Arzerra', *European Medicines Agency* (Web Page, 10 May 2019) <https://www.ema.europa.eu/en/medicines/human/EPAR/arzerra>.
[21] 'Arzerra – Public statement', *European Medicines Agency* (Press Release, 28 February 2019) <https://www.ema.europa.eu/en/documents/public-statement/public-statement-arzerra-withdrawal-marketing-authorisation-european-union_en.pdf>.
[22] 'Kesimpta', *European Medicines Agency* (Web Page, 12 July 2024) <https://www.ema.europa.eu/en/medicines/human/EPAR/kesimpta>.
[23] EP 328 4753 entitled 'Human monoclonal antibodies against CD20 for the treatment of multiple sclerosis'.
[24] C-181/24 *Genmab A/S*, EU:C:2024:627, [17].
[25] C-181/24 *Genmab A/S*, EU:C:2024:627, [26].
[26] C-181/24 *Genmab A/S*, EU:C:2024:627, [27]-[30].

[27] C-181/24 *Genmab A/S*, EU:C:2024:627, [32] citing C-443/17 *Abraxis Bioscience LLC* EU:C:2019:238, [55].
[28] See discussion of the "divisionals game" in the Teva inquiry over Copaxone: 'Antitrust: Commission sends Statement of Objections to Teva over misuse of the patent system and disparagement of rival multiple sclerosis medicine', *European Commission* (Press Release, 10 October 2022) <https://ec.europa.eu/commission/presscorner/detail/en/IP_22_6062>. Further, see C-457/10 *AstraZeneca AB v Commission* EU:C:2012:770 which held that providing misleading information when applying for a SPC could be an abuse of dominant position.
[29] On this see the comments of the Advocate General in C-130/11 *Neurim Pharma*, EU:C:2012:268, [51].